Human Papilloma Viruses (HPV) - Causative Agent of Cervical Cancer

2008 Nobel Prize Medicine (part 1)

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Amidst the prevailing medical beliefs, researches and scientific norms during his time, Harald zur Hausen, proposed a radically different causative agent of cervical cancer, the Human Papilloma Virus or HPV.

Zur Hausen discovered and proved, amidst all the scepticisms, that a previously unrecognized subtype of the HPV, HPV 16 and 18, were consistently found in about 70% of cervical cancer biopsies throughout the world. This discovery gave him the Nobel Prize in “Medicine or Physiology” in 2008 together with Françoise Barré-Sinoussi and Luc Montagnier for the discovery of HIV [1].

The Scientific Paradigm Prior to the Discovery
In the late 1970s, scientists believed that viruses cannot cause cancers. It was a fact back then. In the early 1980s, this was challenged by the prevailing topics of research during that decade. The majority of researches during that decade were about herpes simplex virus type 2 (HSV-2) as the causative agent of cervical cancer. HPV during the 1980's was only known to be the cause of genital warts and not of cervical cancer.

**Dr. Harald Zur Hausen and His Discovery**

As a child born in 1936, Harald zur Hausen already has intensive interest in biology and during that early age, he already wanted to become a scientist. Due to his passion for science, he opted to pursue medicine. Medicine gave him the chance to experience surgery, internal medicine and obstetrics and gynecology. The last part fascinated him the most. He then left the field of medicine and pursued Medical Microbiology and Immunology.

In 1972, he was appointed chairman of the Institute of Clinical Virology in Erlangen-Nürnberg. During this time, he received different reports stating that there exists malignant wart conversion into squamous cell carcinomas, cervical cancer. This then triggered the idea that the cause of genital warts, Human Papilloma Virus or HPV can be the cause of cervical cancer.

In 1974, he conducted a pilot study [2] that revealed that there are different types of papilloma viruses. In the following years, he was able to isolating increasing number of Human Papilloma Virus novel subtypes. In 1979, his co-researchers Lutz Gissmann and Ethel-Michele de Villiers were successful in cloning the first DNA from a genital wart, HPV-6. Following HPV-6, they discovered HPV-11. They used HPV-11 as a probe and one out of 24 cervical cancer biopsies turned out to be positive. In these biopsies, unknown faint bands became visible suggesting that a different subtype of HPV is related to the cancer. The unknown bands were asked to be cloned and in 1983 and 1984, they were able to isolate HPV-16 and HPV-18 respectively.

HPV-16 DNA was found to be present in 50% of all cervical cancer [3] biopsies while HPV-18 was found to be present in 20% of the cases. These figures proved that HPV-16 and 18 play an important role in cervical cancer development.

**Importance of the Discovery**

More than 500,000 women per year are affected by Cervical Cancer. More than 5% of all cancers worldwide are caused by a persistent infection of the Human Papilloma Virus or HPV [4]. There are already more than 100 HPV types that are known to men and 40 of these infect the genital tract, out of the 40, 15 HPV types put women at high risk for cervical cancer. HPV as noted to be seen in 99.7% of all cervical cancers in the world. The discovery of Harald zur Hausen gave us the knowledge about HPV-16 and 18. This discovery paved the way to a greater understanding of cervical cancer. Furthermore, it led to the development of vaccines that are now found to be more than 95% effective in protecting women from HPV acquisition.

**Cervical Cancer**
Vaccines

There are two available vaccines in the market today, Cervarix by GlaxoSmithKline and Gardasil by Merck. Both of these vaccines protect against the infection of both HPV-16 and 18. But Gardasil also protects against HPV-6 and 11 which causes genital warts. These vaccines are recommended to 11 and 12 year-old girls and also to 13-26 year-old females. Both vaccines are delivered 3 times over six months and it is recommended that you take the same brand for the three doses. The vaccines provide little benefits if you are already infected with HPV. It also has no therapeutic effects on existing HPV infections.

Signs and Symptoms

Most people with HPV infections do not manifest symptoms. In more than 90% of infections, the virus is naturally clear from the body within two years. But sometimes, HPV can cause genital warts or worse, cervical cancer. Note that the type of HPV that causes genital warts is different from the type of HPV that causes cervical cancer. Cervical cancers usually do not have symptoms unless it is in the advanced stages. This is the reason why women are advised to get regular cervical cancer screening to detect the cancer during its early stages.

Treatment

There are no treatments available for the virus; treatments are only available for the health problems that it can cause. Cervical cancer, like all the types of cancer is most treatable during its early stages so early diagnosis is the key. Women should get routine cervical cancer screening to detect the cancer even before it develops. The message is prevention is always better than treatment.

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